

Immune-Matched Neural Stem Cell Transplantation for Pediatric Neurodegenerative Disease

Grant Award Details

Immune-Matched Neural Stem Cell Transplantation for Pediatric Neurodegenerative Disease

Grant Type: Early Translational III

Grant Number: TR3-05476

Project Objective: This aim of the program is to develop a DC to treat a lysosomal storage disease (LSD), an inherited fatal disease of young children that results from an enzyme deficiency. Pediatric genetic neurodegenerative diseases, such as the LSDs, account for a large burden of mortality and morbidity in young children. Hematopoietic stem cell transplant (HSCT) can ameliorate peripheral symptoms in these diseases by replacing the defecting enzyme peripherally, but does not treat the deadly neurodegenerative process. The proposed approach is - targeting peripheral organs with HSCT and neurodegeneration with a second stem cell transplant (SCT) into the central nervous system - is mandatory for whole-body treatment of a systemic disease. Further, our approach will obviate pharmacologic immunosuppression.

Investigator:

Name: Philip Schwartz
Institution: Children's Hospital of Orange County
Type: PI

Name: Patricia Dickson
Institution: University of California, Los Angeles
Type: Co-PI

Disease Focus: Neurological Disorders, Pediatrics

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: \$4,266,015

Status: Closed

Progress Reports

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Grant Application Details

Application Title:	Immune-Matched Neural Stem Cell Transplantation for Pediatric Neurodegenerative Disease
Public Abstract:	<p>Children with inherited degenerative diseases of the brain will be among the first to benefit from novel approaches based on stem cell therapy (SCT). This assertion is based on a number of medical and experimental observations and precedents including:</p> <ol style="list-style-type: none"> 1) These diseases currently lack effective therapies and can cause profound mental retardation or lead to death; 2) SCT has already been shown to work in the milder forms of similar diseases that do not affect the brain; 3) Experimental work and early clinical studies have clearly shown that stem cells delivered directly into the brain can be used to treat diseases affecting the brain; and 4) The clinical safety of stem cells delivered directly into the brain has already been established during recent Phase 1 clinical trials. <p>Our approach is designed to lead to a therapeutic development candidate, based on stem cells, by addressing two critical issues: (i) that early intervention is not only required but is indeed possible in this patient population and that, (ii) induction of immune tolerance is also required. We not only address these two important issues but also set the stage for efficient translation of our approach into clinical practice, by adapting transplant techniques that are standard in clinical practice or in clinical trials and using laboratory cell biology methods that are easily transferrable to the scale and processes of clinical cell manufacturing.</p>

Statement of Benefit to California: We are focusing on a class of childhood brain diseases that causes a child's brain to degenerate and results in severe mental retardation or death, in addition to damage to many other organ systems. These diseases are not yet represented in CIRM's portfolio. Recently blood stem cell transplantation has been applied to these diseases, showing that some of the organ systems can be rescued by stem cell therapy. Unfortunately, the brain component of the disease is not impacted by blood stem cell therapy. Our team proposes to take these important lessons to develop a therapy that treats all organ dysfunction, including brain. Because of the established stem cell success in the clinical treatment of non-brain organs and the experimental treatment of the brain, we propose a novel, combined stem cell therapy. Based on our own work and recent clinical experience, this dual stem cell therapy has a high probability of success for slowing or reversing disease, and importantly, will not require children to be treated with toxic immunosuppressive drugs. This therapy will thus benefit California by: 1) reducing disease burden in individuals and the State's burden for caring for these children; 2) providing a successful model of stem cell therapy of the brain that will both bolster public confidence in CIRM's mission to move complex stem cell therapies into the clinic; and 3) laying the groundwork for using this type of therapy with other brain diseases of children.

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